

REMARKS


Applicants have canceled claims 2, 3, 6-15, 23, 28, 34-36, 44-47, 55-58, and 63. Independent claims 1, 43, 52, and 53 have been amended to incorporate the limitations of claim 3. Dependent claims 4, 5, 17, 18, and 61 have been amended to recite that the polypeptide further comprises substitutions at particular positions. Support for these amendments can be found throughout the specification, including for example, at page 12, line 24 through page 13, line 8 of the published PCT. Independent claims 59, 70, and 73 have been amended to recite that the substitution is at residue 34, 35, or 36. Support for this amendment can be found throughout the specification, including, for example, at page 13, lines 4-8 of the published PCT.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be examined. Enclosed is a check for excess claim fees. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

Claims 2, 3, 6-15, 23, 28, 34-36, 44-47, 55-58, and 63 have been canceled.

Claims 1, 4-5, 17-18, 43, 53-54, 59, 61, 67, 70, and 73 have been amended as follows.

1. (Amended) A vitamin K-dependent polypeptide comprising a modified GLA domain that enhances membrane binding affinity and activity of said polypeptide relative to a corresponding native vitamin K-dependent polypeptide, said modified GLA domain comprising at least one amino acid substitution at amino acid 5, 9, 35, or 36, wherein said polypeptide is one that inhibits clot formation.

4. (Amended) The polypeptide of claim 1, wherein said amino acid substitution [is at] further comprises an amino acid substitution at amino acid 11 or 12.

5. (Amended) The polypeptide of claim 1, wherein said amino acid substitution [is at] further comprises an amino acid substitution at amino acid 29 or 33.

17. (Amended) The polypeptide of claim 16, wherein said polypeptide further comprises a glutamic acid at amino acid 33.

18. (Amended) The polypeptide of claim 16, wherein said amino acid substitution further comprises a glutamine residue at amino acid 11 and a glutamic acid residue at amino acid 33.

43. (Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and an effective amount of a vitamin K-dependent polypeptide, wherein said vitamin K-dependent polypeptide comprises a modified GLA domain that enhances membrane

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binding affinity and activity of said polypeptide relative to a corresponding native vitamin K-dependent polypeptide, said modified GLA domain comprising at least one amino acid substitution at amino acid 5, 9, 35, or 36, and wherein said vitamin K-dependent polypeptide inhibits clot formation.

52. (Amended) A mammalian host cell comprising a vitamin K-dependent polypeptide, said vitamin K-dependent comprising a modified GLA domain that enhances membrane binding affinity and activity of said polypeptide relative to a corresponding native vitamin K-dependent polypeptide, said modified GLA domain comprising at least one amino acid substitution at amino acid 5, 9, 35, or 36, wherein said polypeptide is one that inhibits clot formation.

53. (Amended) A method of decreasing clot formation in a mammal comprising administering an amount of a vitamin K-dependent polypeptide effective to decrease clot formation in said mammal, wherein said vitamin K-dependent polypeptide comprises a modified GLA domain that enhances membrane binding affinity and activity of said polypeptide relative to a corresponding native vitamin K-dependent polypeptide, said modified GLA domain comprising at least one amino acid substitution at amino acid 5, 9, 35, or 36.

54. (Amended) The method of claim 53, wherein said polypeptide is [Protein C or Activated protein C,] active-site modified Factor VIIa, active-site modified Factor IXa, or Protein S.

59. (Amended) A Factor VII or Factor IX polypeptide comprising a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor IX polypeptide, said modified GLA domain comprising at least one amino acid substitution at residue [11, 29, 34, or 35] 34, 35, or 36.

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61. (Amended) The polypeptide of claim 60, wherein said amino acid substitution further comprises a glutamine, a glutamic acid, an aspartic acid, or an asparagine residue [is substituted] at amino acid 11.

67. (Amended) The polypeptide of claim 60, wherein said modified GLA domain [further] comprises at least one hydrophobic residue at residue 34 or 35.

70. (Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and an amount of a Factor VII or Factor IX polypeptide effective to increase clot formation in a mammal, wherein said Factor VII or Factor IX polypeptide comprises a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor IX polypeptide, said modified GLA domain comprising at least one amino acid substitution at residue [11, 29, 34, or 35] 34, 35, or 36.

73. (Amended) A method of increasing clot formation in a mammal comprising administering an amount of a Factor VII or Factor IX polypeptide effective to increase clot formation in said mammal, wherein said Factor VII or Factor IX polypeptide comprises a modified GLA domain that enhances membrane binding affinity of said polypeptide relative to a corresponding native Factor VII or Factor IX polypeptide, said modified GLA domain comprising at least one amino acid substitution at residue [11, 29, 34, or 35] 34, 35, or 36.

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